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Attorney Docket No. P66566US0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Roger NITSCH et al.

Application No.: 09/831,754 Art Unit: 1646

Filed: October 15, 2001 Examiner: Olga N. Chernyshev

For METHODS OF DIAGNOSING OR TREATING NEUROLOGICAL DISEASE

AMENDMENT

Commissioner for Patents
United States Patent and Trademark Office
Washington, D.C. 20231

Sir:

The instant paper responds to the PTO notice mailed March 24, 2003.

IN THE SPECIFICATION

At page 1, immediately following the title, insert:

B1 This is a 371 of PCT/EP99/08744, filed November 12, 1999, and published in English.

Rewrite the paragraph bridging pages 24 and 25 as:

B2 Figure 16 shows the amino acid sequence (SEQ ID NO: 1) of SELADIN-1. A differential display approach (von der Kammer, H. et al., Nucleic acid research, 27, 2211, 1999; von der Kammer, H. et al., J. Biol. Chem. 273, 14538, 1998) to identify genes that are differentially expressed in selectively vulnerable cell populations in the inferior temproal cortex with confirmed neurodegeneration and in the largely unaffected frontal or sensory-motor cortex of the same subject in three brains with a histopathological diagnosis of Alzheimer's disease and post mortem time intervals of less than four hours. By using forty different primer combinations, twenty-eight of thirty-six differentially expressed cDNAs were cloned and sequenced. These cDNAs were further analyzed by reverse Northern blotting (Poirier G.M.-C. et al., Nucleic Acid Res., 25, 913, 1997; Van Gelder R. N. et al., Proc. Natl. Acad. Sci. USA, 87, 1663, 1990) to confirm differential expression between the two AD brain regions. Expression of one of these cDNAs was markedly lower in the inferior

temporal lobe than in the sensory-motor cortex. Therefore, the potential importance of this transcript for the selective vulnerability in AD brain has been investigated. The cDNA sequence consisted of 4248 nucleotides and encoded an open reading frame of 516 amino acid residues. Due to a cytidine insertion at nucleotide position 1167, this sequence differed from the much shorter coding region of its homolog KIAA0018 deposited in GenBank (Nomura et al., D N A Res. 1, 27, 1994; GenBank database accession HUMRSC390D13643,1, 1992; DIMH Human Q15392, 1998). The new gene has been designated SELADIN-1. The homology domain to oxido-reductases are highlighted in red; the homologies to "diminuto like proteins" of other species are underlined. The first 21 amino acid residues represent a putative signal peptide. One possible caspase recognition motif is highlighted in yellow. This putative caspase recognition motif "LEVD" is present within the SELADIN-1 amino acid sequence at position 121 - 125. *In vitro* cleavage of SELADIN-1 by caspase 3 or 6 generated four different SELADIN-1 fragments of approximately 50, 40, 30 and 20 kDa, respectively. Secondary structure predictions revealed at least four possible transmembrane domains.

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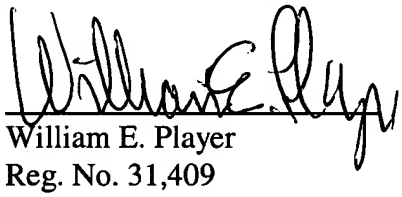
REMARKS

The specification is amended, hereby, to include the §371 priority and to insert the sequence identifier corresponding to the amino acid sequence disclosed in Fig. 16. The requisite marked-up version of the amendments is attached hereto.

Favorable action is requested.

Respectfully submitted,

JACOBSON·HOLMAN PLLC

By: 

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